

**Application No.: 10/531,435**  
**Filing Date: October 7, 2005**

**AMENDMENTS TO THE DRAWINGS**

The attached sheets of drawings include changes to Figures 5-9, 13 and 14. These sheets, which include Figures 5-10, 13 and 14, replaces the original sheets including Figures 5-10, 13 and 14. In Figures 5-9, the term "SMH" has been spelled out for consistency with Figure 10. In Figures 13 and 14, previously omitted index and unit for the horizontal axis has been added.

Attachment: Replacement Sheets

### REMARKS

Claims 19-51 are currently pending in the application. Claim 1 has been amended. Claims 22, 25, 26, 28, 29, 32, 35, 36, 44-51 have been canceled without prejudice or disclaimer. Support for the amendments can be found throughout the specification and claims as originally filed. In addition, the specification and drawings have been amended as indicated above. No new matter has been introduced with the foregoing amendments. Entry of the amendments to the specification and claims and replacement sheets of drawings and reconsideration is respectfully requested.

#### Objection to the Specification

The Examiner found that at page 2, line 20, the meaning of "Ser(P)" is not apparent. Applicants respectfully note that a skilled artisan would immediately recognize the commonly known term "Ser(P)" as referring to phosphoserine. Nevertheless, Applicants have amended the specification to clarify that "Ser(P)" is phosphoserine.

The Examiner has requested that "MAP" should be spelled out for the first instance of use. Applicants respectfully note that "MAP" is part of the given name "MAP 112" of a phosphoprotein identified as discussed in the specification, and spelling out of MAP is inapplicable. However, for clarification, *Applicants* have amended the specification to indicate that the "MAP 112" phosphoprotein solution referred to in Figure 5 is prepared by the method of Example 4 of the specification.

The Examiner has requested a definition for "Novo.45K" and "USP." Applicants have amended the last paragraph on page 12 to clarify that "Novo.4500K" is a product from the company Novozymes®, and "USP" stands for (United States Pharmacopaeia), as is well-known in the art.

The Examiner has requested that at page 19, line 16, "280 nm" be changed to "280 nm." Applicants have amended the specification accordingly.

The Examiner objected to page 32, lines 18-21 as setting for four molecular weight ranges with "unit." Applicants have amended the specification as indicated above to include units as required.

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As no new matter has been introduced by the foregoing amendments to the specification, Applicants respectfully request their entry into the application.

**Objection to the Claims**

The Examiner objected to Claim 50 for recitation of the phrase “y the partial hydrolysis.” In addition, Claim 45 was objected to for the phrase “comprises about 10 or more  $\mu\text{mol}$ .” Claims 50 and 45 have been canceled without prejudice, thereby obviating the objection.

**Objection to the Drawings**

The Examiner objected to Figures 5-9 for not spelling out “SMH.” Replacement sheets including Figures 5-10 have been submitted herewith. The replacement sheets contain amended Figures 5-9 where “SMH” has been spelled out as “Surface microhardness” as shown in Figure 10.

Figures 13-15 have been objected to for lacking an index and units for the horizontal axis. A replacement sheet including Figures 13-14 have been submitted herewith. The replacement sheet contains Figures 13-14, which have been amended to include the index and unit “phosphoprotein concentration (% w/w)”. Support for the amendment can be found at, for example, the first two paragraphs of page 9 of the specification as originally filed

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 19-43 and 45-51 have been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Without acquiescing in the rejection, solely to expedite prosecution Applicants have canceled Claims 45-51 without prejudice, thereby obviating the rejection of Claims 45-51.

With regard to Claim 19, the Examiner found that the recitation of “phosphoprotein preparation has been obtained by partially cross linking...” is unclear whether or not said preparation actually comprises the crosslinked phosphoprotein and/or non-crosslinked phosphoprotein. Without acquiescing in the rejection, solely to expedite prosecution Applicants have amended independent Claim 19 to clarify that the composition “comprises a partially cross-linked partial hydrolysate of casein or a caseinate” and that the phosphoprotein preparation has “a degree of cross-linking of between 10 $\mu\text{mol}$  and 250 $\mu\text{mol}$  cross-links per gram of the total

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phosphoprotein in the preparation.” As such, it is clear that the preparation comprises a partially cross-linked partial hydrolysate of casein or a caseinate.

Claim 22 has been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that the recitation of “total number of peptide bond” is unclear as to which proteins the peptides bonds refer. Claim 22 has been canceled, thereby rendering the rejection of Claim 22 moot.

Claims 23 and 24 have been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that it was unclear what the subject of “about 3.5% to about 7%” and “about 4% to about 6.5%” is. Applicants have amended Claims 23 and 24 to clarify that the subject of the recited clauses is the total number of peptide bonds in the casein or caseinate. Withdrawal of the indefiniteness rejection is respectfully requested.

Claim 25 has been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that the metes and bounds of “or less” is unclear as to whether or not 0% is included. Without acquiescing in the rejection, solely to expedite prosecution Applicants have canceled Claim 25 without prejudice, thereby obviating the rejection.

Claim 28 has been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that the upper limit of “or more” is unclear. The Examiner also found that “per gram of protein” was unclear as to what protein is being referred to. Without acquiescing in the rejection, solely to expedite prosecution Applicants have canceled Claim 28 without prejudice, thereby obviating the rejection.

Claim 34 has been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that the recitation of “milk calcium” is vague and awkward because neither the specification nor the relative art defines or teaches “milk calcium.” Without acquiescing in the rejection, solely to expedite prosecution Applicants have amended Claim 34 to clarify that the composition includes calcium from natural milk and removing the recitation of “milk calcium,” thereby rendering the rejection moot.

Claim 37 has been rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. The Examiner found that the metes and bounds of the recited limitation ranges

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are ambiguous. Applicants believe that it is clear that milk calcium refers to calcium from milk. Nevertheless, without acquiescing in the rejection, solely to expedite prosecution Applicants have amended Claim 37 to clarify delete the recitation of "about," thereby rendering the rejection moot.

In view of the amendment and above remarks, the pending claims are not indefinite. Withdrawal of the indefiniteness rejection is respectfully requested.

**Rejections Under 35 U.S.C. § 102**

*Lauber et al.*

Claims 19-27, 31-34, 37-38 and 45-48 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lauber *et al.* (*Nahrung/Food* (2001, June) 45, 215-217). According to the Examiner, Lauber *et al.* teach a UHT milk containing cross-linked casein (casein oligomerization). To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See, Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitation so flte claim are found within a single prior art reference... There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See, Scripps Clinic & Research Foundation v. Genentech, Inc.* 927 F.2d 1565 (Fed. Cir. 1991). Lauber *et al.* fail to teach each and very element of the claimed invention.

Applicants have found that, surprisingly, phosphoproteins obtained by partially cross-linking a partial hydrolysate of casein or caseinate have advantageous properties that make them useful in remineralising tooth enamel and for preventing or treating dental caries, tooth erosion, dental hypersensitivity and gingivitis. The phosphoprotein preparations taught by Applicants have been found to have an increased solubility in the presence of divalent cations and an increased ability to bind such cations when compared to non-cross-linked partially hydrolyzed casein.

Applicants have amended Claim 19 to clarify that the composition "comprises an effective amount of a phosphoprotein preparation in combination with one or more carriers or diluents, wherein the phosphoprotein preparation comprises a partially cross-linked partial hydrolysate of casein or a caseinate, wherein the partially cross-linked partial hydrolysate has been obtained by partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate, wherein the partially hydrolyzing step is followed by partially cross-linking the partially hydrolysed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation; a source of calcium ions; and a source of phosphate ions, or a source of strontium ions." In addition, Applicants have canceled Claims 45-51 without prejudice. Claims 20-27, 31-34 and 37-38 each ultimately depend from independent Claim 19.

The Lauber *et al.* reference relates to a study of the effect of irreversible oligomerization of casein occurring during the storage of UHT milk on the resulting yogurt gel-forming properties. See, Lauber *et al.* at page 215, last paragraph of the Introduction. Lauber *et al.* disclose that non-enzymatic casein crosslinking increases during storage of UHT milk. See, Lauber *et al.* at page 216, col. 1, first paragraph under Results and Discussion. Lauber *et al.* do not disclose a "partially cross-linked partial hydrolysate of casein or a caseinate, wherein the partially cross-linked partial hydrolysate has been obtained by partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate, wherein the partially hydrolyzing step is followed by partially cross-linking the partially hydrolysed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation" as recited by amended Claim 19. Further, Lauber *et al.* do not inherently disclose such a partially cross-linked partial hydrolysate of casein or a caseinate.

With regard to establishing inherency of a certain result, the M.P.E.P. sets forth the following:

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is **necessarily present** in the

thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The *mere fact that a certain thing may result from a given set of circumstances is not sufficient.*" *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)

M.P.E.P. § 2112(IV), emphasis added.

Lauber *et al.* do *not* inherently disclose the partially cross-linked partial hydrolysate of casein or a caseinate as recited by amended Claim 19 for at least the following reasons. First, Lauber *et al.* do *not* inherently disclose partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate. One of skill in the art would clearly recognize that the mere presence of endogenous trypsin in the UHT milk would not *necessarily* result in partial hydrolysis of casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate. As clearly set forth in the M.P.E.P. excerpt above, the mere fact that a certain thing *may* result (e.g., hydrolysis of 3% to 89%) from a given set of circumstances is *not sufficient* to establish inherency of the specific degree of hydrolysis. Second, Lauber *et al.* do not inherently disclose subsequently partially cross-linking the partially hydrolyzed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation. Thus, the partially cross-linked partial hydrolysate of casein or a caseinate "obtained by partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate, wherein the partially hydrolyzing step is followed by partially cross-linking the partially hydrolysed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation" is *not necessarily* present in the yogurt disclosed by Lauber. Therefore, Lauber *et al.* do *not* inherently disclose the claimed composition.

Thus, Lauber *et al.* do not disclose all of the limitations of Claim 19, and as such, do not anticipate Claim 19 and the claims depending therefrom. Applicants respectfully request withdrawal of the § 102(b) and allowance of the pending claims.

*Reynolds (U.S. Patent No. 5,981,475)*

Claims 19-26, 31-34 and 37-43 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Reynolds (U.S. Patent No. 5,981,475, hereinafter the “‘475 Patent”). According to the Examiner, Reynolds teaches a dentinal composition comprising a casein prepared by hydrolysis. The Examiner found that the ‘475 Patent teaches Claims 19-20 because “the composition of instant claim 19, as written, does not necessarily comprise the cross-linked casein. To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

As an initial matter, Applicants note that the Examiner has acknowledged that Claims 45 and dependent claims therefrom are *not* anticipated by the ‘475 Patent, because they are directed to a phosphoprotein preparation comprising the cross-linked phosphoprotein. *See*, page 12 of the Office Action, lines 1-3.

As discussed above, Applicants have amended Claim 19 to clarify that the composition “comprises an effective amount of a phosphoprotein preparation in combination with one or more carriers or diluents, wherein the phosphoprotein preparation comprises a partially cross-linked partial hydrolysate of casein or a caseinate, wherein the partially cross-linked partial hydrolysate has been obtained by partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate, wherein the partially hydrolyzing step is followed by partially cross-linking the partially hydrolysed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation; a source of calcium ions; and a source of phosphate ions, or a source of strontium ions.” Thus, the claimed composition comprises “a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation.” Claims 20-26, 31-34 and 37-43 each ultimately depend from independent Claim 19.

The ‘475 Patent discloses peptides obtained by hydrolysis of casein, *without any subsequent cross-linking*. At no point does the ‘475 Patent disclose, teach or suggest that the

peptides obtained by hydrolysis are subsequently partially cross-linked. In contrast, Claim 19 recites that the composition comprises, *inter alia*, “a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation.” Thus, the ‘475 Patent does not disclose all of the limitation of Claim 19, and as such, does not anticipate Claim 19 and the claims depending therefrom. Applicants respectfully request withdrawal of the § 102(b) and allowance of the pending claims.

*Reynolds (U.S. Patent No. 5,130,123)*

Claims 19-26, 31-34 and 43 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Reynolds (U.S. Patent No. 5,130,123, hereinafter the “‘123 Patent”). According to the Examiner, Reynolds teaches a dentinal composition comprising a casein prepared by hydrolysis. The Examiner found that the ‘123 Patent teaches Claims 19-20 because “the composition of instant claim 19, as written, does not necessarily comprise the cross-linked casein. To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

As discussed above, Applicants have amended Claim 19 to clarify that the composition “comprises an effective amount of a phosphoprotein preparation in combination with one or more carriers or diluents, wherein the phosphoprotein preparation comprises a partially cross-linked partial hydrolysate of casein or a caseinate, wherein the partially cross-linked partial hydrolysate has been obtained by partially hydrolysing casein or a caseinate to a degree of hydrolysis of about 3% to about 89% of the total number of peptide bonds in the casein or caseinate, wherein the partially hydrolyzing step is followed by partially cross-linking the partially hydrolysed casein or caseinate to produce a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation; a source of calcium ions; and a source of phosphate ions, or a source of strontium ions.” Thus, the claimed composition comprises “a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation.” Claims 20-26, 31-34 and 43 each ultimately depend from independent Claim 19.

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The '123 Patent discloses peptides obtained by hydrolysis of casein, without any subsequent cross-linking. At no point does the '123 Patent disclose, teach or suggest that the peptides obtained by hydrolysis are subsequently partially cross-linked. In contrast, Claim 19 recites that the composition comprises, *inter alia*, "a phosphoprotein preparation having a degree of cross-linking of between 10 $\mu$ mol and 250 $\mu$ mol cross-links per gram of the total phosphoprotein in the preparation." Thus, the '123 Patent does not disclose all of the limitation of Claim 19, and as such, does not anticipate Claim 19 and the claims depending therefrom. Applicants respectfully request withdrawal of the § 102(b) and allowance of the pending claims.

### Conclusion

For the foregoing reasons, it is respectfully submitted that the rejections set forth in the outstanding Office Action have been addressed and that the application is in condition for allowance. Accordingly, Applicants request the expeditious allowance of the pending claims.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call the undersigned to discuss such issues.

### No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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